04CO

OIPE

RAW SEQUENCE LISTING DATE: 11/29/2000
PATENT APPLICATION: US/09/711,022 TIME: 09:12:34

ENTERED

Input Set : A:\V1397028.txt
Output Set: N:\CRF3\11292000\I711022.raw

```
      4 <110> APPLICANT: MARTHA K. NEWELL
      7 <120> TITLE OF INVENTION: METHODS AND PRODUCTS RELATED TO
      8       METABOLIC INTERACTIONS IN DISEASE
     11 <130> FILE REFERENCE: V0139/7028
C--> 13 <140> CURRENT APPLICATION NUMBER: US/09/711,022
C--> 13 <141> CURRENT FILING DATE: 2000-11-09
     13 <150> PRIOR APPLICATION NUMBER: U.S. 60/082,250
     14 <151> PRIOR FILING DATE: 1998-04-17
     16 <150> PRIOR APPLICATION NUMBER: U.S. 60/094,519
     17 <151> PRIOR FILING DATE: 1998-07-29
     19 <150> PRIOR APPLICATION NUMBER: U.S. 60/101,580
     20 <151> PRIOR FILING DATE: 1998-09-24
     22 <160> NUMBER OF SEQ ID NOS: 13
     24 <170> SOFTWARE: FastSEQ for Windows Version 3.0
     26 <210> SEQ ID NO: 1
     27 <211> LENGTH: 1491
     28 <212> TYPE: DNA
     29 <213> ORGANISM: Homo Sapiens
     31 <400> SEQUENCE: 1
     32  ccaaagaaaa agtgatttgt cattgcttta tagactgtaa gaagagaaca tctcagaagt      60
     33  ggagtcttac cctgaaatca aaggatttaa agaaaaagtg gaattttttt tcagcaagct     120
     34  gtgaaactaa atccacaacc tttggagacc caggaacacc ctccaatctc tgtgtgtttt     180
     35  gtaaacatca ctggagggtc ttctacgtga gcaattggat tgtcatcagc cctgccctgtt     240
     36  ttgcacctgg gaagtgccct ggtcttactt gggtccaaat tgttggcttt cacttttgac     300
     37  cctaagcatc tgaagccatg ggccacacac ggaggcaggg aacatcacca tccaagtgtc     360
     38  catacctcaa tttctttcag ctcttggtgc tggctggtct ttctcacttc tgttcaggtg     420
     39  ttatccacgt gaccaaggaa gtgaaagaag tggcaacgct gtcctgtggt cacaatgttt     480
     40  ctgttgaaga gctggcacaa actcgcatct actggcaaaa ggagaagaaa atggtgctga     540
     41  ctatgatgtc tggggacatg aatatatggc ccgagtacaa gaaccggacc atctttgata     600
     42  tcactaataa cctctccatt gtgatcctgg ctctgcgccc atctgacgag ggcacatacg     660
     43  agtgtgttgt tctgaagtat gaaaaagacg ctttcaagcg ggaacacctg gctgaagtga     720
     44  cgttatcagt caaagctgac ttccctacac ctagtatatc tgactttgaa attccaactt     780
     45  ctaatattag aaggataatt tgctcaacct ctggaggttt tccagagcct cacctctcct     840
     46  ggttggaaaa tggagaagaa ttaaatgcca tcaacacaac agtttcccaa gatcctgaaa     900
     47  ctgagctcta tgctgttagc agcaaactgg atttcaatat gacaaccaac cacagcttca     960
     48  tgtgtctcat caagtatgga catttaagag tgaatcagac cttcaactgg aatacaacca    1020
     49  agcaagagca ttttcctgat aacctgctcc catcctgggc cattaccttа atctcagtaa    1080
     50  atggaatttt tgtgatatgc tgcctgacct actgctttgc cccaagatgc agagagagaa    1140
     51  ggaggaatga gagattgaga agggaaagtg tacgccctgt ataacagtgt ccgcagaagc    1200
     52  aaggggctga aaagatctga aggtagcctc cgtcatctct tctgggatac atggatcgtg    1260
     53  gggatcatga ggcattcttc ccttaacaaa tttaagctgt ttttacccact acctcacctt    1320
     54  cttaaaaacc tctttcagat taagctgaac agttacaaga tggctggcat ccctctcctt    1380
     55  tctccccata tgcaatttgc ttaatgtaac ctctttcttt gccatgtttc cattctgcca    1440
     56  tcttgaattg tcttgtcagc cnattcatta tctattaaac actaatttga g              1491
     58 <210> SEQ ID NO: 2
     59 <211> LENGTH: 288
     60 <212> TYPE: PRT
```

RAW SEQUENCE LISTING DATE: 11/29/2000
PATENT APPLICATION: US/09/711,022 TIME: 09:12:34

Input Set : A:\V1397028.txt
Output Set: N:\CRF3\11292000\I711022.raw

<213> ORGANISM: Homo Sapiens
<400> SEQUENCE: 2

Met	Gly	His	Thr	Arg	Arg	Gln	Gly	Thr	Ser	Pro	Ser	Lys	Cys	Pro	Tyr
1				5				10					15		
Leu	Asn	Phe	Phe	Gln	Leu	Leu	Val	Leu	Ala	Gly	Leu	Ser	His	Phe	Cys
			20					25					30		
Ser	Gly	Val	Ile	His	Val	Thr	Lys	Glu	Val	Lys	Glu	Val	Ala	Thr	Leu
		35					40					45			
Ser	Cys	Gly	His	Asn	Val	Ser	Val	Glu	Glu	Leu	Ala	Gln	Thr	Arg	Ile
	50					55					60				
Tyr	Trp	Gln	Lys	Glu	Lys	Lys	Met	Val	Leu	Thr	Met	Met	Ser	Gly	Asp
65					70					75					80
Met	Asn	Ile	Trp	Pro	Glu	Tyr	Lys	Asn	Arg	Thr	Ile	Phe	Asp	Ile	Thr
				85					90					95	
Asn	Asn	Leu	Ser	Ile	Val	Ile	Leu	Ala	Leu	Arg	Pro	Ser	Asp	Glu	Gly
			100					105					110		
Thr	Tyr	Glu	Cys	Val	Val	Leu	Lys	Tyr	Glu	Lys	Asp	Ala	Phe	Lys	Arg
		115					120					125			
Glu	His	Leu	Ala	Glu	Val	Thr	Leu	Ser	Val	Lys	Ala	Asp	Phe	Pro	Thr
	130					135					140				
Pro	Ser	Ile	Ser	Asp	Phe	Glu	Ile	Pro	Thr	Ser	Asn	Ile	Arg	Arg	Ile
145					150					155					160
Ile	Cys	Ser	Thr	Ser	Gly	Gly	Phe	Pro	Glu	Pro	His	Leu	Ser	Trp	Leu
				165					170					175	
Glu	Asn	Gly	Glu	Glu	Leu	Asn	Ala	Ile	Asn	Thr	Thr	Val	Ser	Gln	Asp
			180					185					190		
Pro	Glu	Thr	Glu	Leu	Tyr	Ala	Val	Ser	Ser	Lys	Leu	Asp	Phe	Asn	Met
		195					200					205			
Thr	Thr	Asn	His	Ser	Phe	Met	Cys	Leu	Ile	Lys	Tyr	Gly	His	Leu	Arg
	210					215					220				
Val	Asn	Gln	Thr	Phe	Asn	Trp	Asn	Thr	Thr	Lys	Gln	Glu	His	Phe	Pro
225					230					235					240
Asp	Asn	Leu	Leu	Pro	Ser	Trp	Ala	Ile	Thr	Leu	Ile	Ser	Val	Asn	Gly
				245					250					255	
Ile	Phe	Val	Ile	Cys	Cys	Leu	Thr	Tyr	Cys	Phe	Ala	Pro	Arg	Cys	Arg
			260					265					270		
Glu	Arg	Arg	Arg	Asn	Glu	Arg	Leu	Arg	Arg	Glu	Ser	Val	Arg	Pro	Val
		275					280					285			

<210> SEQ ID NO: 3
<211> LENGTH: 1424
<212> TYPE: DNA
<213> ORGANISM: Homo Sapiens
<400> SEQUENCE: 3

aggagcctta ggaggtacgg ggagctcgca aatactcctt ttggttttatt cttaccacct 60
tgcttctgtg ttccttggga atgctgctgt gcttatgcat ctggtctctt tttggagcta 120
cagtggacag gcatttgtga cagcactatg ggactgagta acattctctt tgtgatggcc 180
ttcctgctct ctggtgctgc tcctctgaag attcaagctt atttcaatga gactgcagac 240
ctgccatgcc aatttgcaaa ctctcaaaac caaagcctga gtgagctagt agtatttttgg 300
caggaccagg aaaacttggt tctgaatgag gtatacttag gcaaagagaa atttgacagt 360

RAW SEQUENCE LISTING DATE: 11/29/2000
PATENT APPLICATION: US/09/711,022 TIME: 09:12:34

Input Set : A:\V1397028.txt
Output Set: N:\CRF3\11292000\I711022.raw

```
113  gttcattcca agtatatggg ccgcacaagt tttgattcgg acagttggac cctgagactt     420
114  cacaatcttc agatcaagga caagggcttg tatcaatgta tcatccatca caaaaagccc     480
115  acaggaatga ttcgcatcca ccagatgaat tctgaactgt cagtgcttgc taacttcagt     540
116  caacctgaaa tagtaccaat ttctaatata acagaaaatg tgtacataaa tttgacctgc     600
117  tcatctatac acggttaccc agaacctaag aagatgagtg ttttgctaag aaccaagaat     660
118  tcaactatcg agtatgatgg tattatgcag aaatctcaag ataatgtcac agaactgtac     720
119  gacgtttcca tcagcttgtc tgtttcattc cctgatgtta cgagcaatat gaccatcttc     780
120  tgtattctgg aaactgacaa gacgcggctt ttatcttcac ctttctctat agagcttgag     840
121  gaccctcagc ctcccccaga ccacattcct tggattacag ctgtacttcc aacagttatt     900
122  atatgtgtga tggttttctg tctaattcta tggaaatgga agaaggaaga gcggcctcgc     960
123  aactcttata aatgtggaac caacacaatg gagagggaag agagtgaaca gaccaagaaa    1020
124  agagaaaaaa tccatatacc tgaaaagatct gatgaagccc agcgtgtttt taaaagttcg    1080
125  aagacatctt catgcgacaa aagtgataca tgtttttaat taaagagtaa agcccataca    1140
126  agtattcatt ttttctaccc tttcctttgt aagttcctgg gcaaccttttt tgatttcttc    1200
127  cagaaggcaa aaagacatta ccatgagtaa taaggggcct ccaggactcc ctctaagtgg    1260
128  aataqcctcc ctgtaactcc agctctgctc cgtatgccaa gaggagactt taattctctt    1320
129  actgcttctt ttcacttcag agcacactta tgggccaagc ccagcttaat ggctcatgac    1380
130  ctggaaataa aatttaggac caataaaaaa aaaaaaaaaa aaaa                     1424
132 <210> SEQ ID NO: 4
133 <211> LENGTH: 323
134 <212> TYPE: PRT
135 <213> ORGANISM: Homo Sapiens
137 <400> SEQUENCE: 4
138  Met Gly Leu Ser Asn Ile Leu Phe Val Met Ala Phe Leu Leu Ser Gly
139   1               5                  10                  15
140  Ala Ala Pro Leu Lys Ile Glu Ala Tyr Phe Asn Glu Thr Ala Asp Leu
141              20                  25                  30
142  Pro Cys Gln Phe Ala Asn Ser Gln Asn Gln Ser Leu Ser Glu Leu Val
143          35                  40                  45
144  Val Phe Trp Gln Asp Gln Glu Asn Leu Val Leu Asn Glu Val Tyr Leu
145      50                  55                  60
146  Gly Lys Glu Lys Phe Asp Ser Val His Ser Lys Tyr Met Gly Arg Thr
147  65                  70                  75                  80
148  Ser Phe Asp Ser Asp Ser Trp Thr Leu Arg Leu His Asn Leu Gln Ile
149                  85                  90                  95
150  Lys Asp Lys Gly Leu Tyr Gln Cys Ile Ile His His Lys Lys Pro Thr
151              100                 105                 110
152  Gly Met Ile Arg Ile His Gln Met Asn Ser Glu Leu Ser Val Leu Ala
153          115                 120                 125
154  Asn Phe Ser Gln Pro Glu Ile Val Pro Ile Ser Asn Ile Thr Glu Asn
155      130                 135                 140
156  Val Tyr Ile Asn Leu Thr Cys Ser Ser Ile His Gly Tyr Pro Glu Pro
157  145                 150                 155                 160
158  Lys Lys Met Ser Val Leu Leu Arg Thr Lys Asn Ser Thr Ile Glu Tyr
159                  165                 170                 175
160  Asp Gly Ile Met Gln Lys Ser Gln Asp Asn Val Thr Glu Leu Tyr Asp
161              180                 185                 190
162  Val Ser Ile Ser Leu Ser Val Ser Phe Pro Asp Val Thr Ser Asn Met
163          195                 200                 205
```

RAW SEQUENCE LISTING DATE: 11/29/2000
PATENT APPLICATION: US/09/711,022 TIME: 09:12:34

Input Set : A:\V1397028.txt
Output Set: N:\CRF3\11292000\I711022.raw

```
164  Thr Ile Phe Cys Ile Leu Glu Thr Asp Lys Thr Arg Leu Leu Ser Ser
165      210                 215                 220
166  Pro Phe Ser Ile Glu Leu Glu Asp Pro Gln Pro Pro Pro Asp His Ile
167  225                 230                 235                 240
168  Pro Trp Ile Thr Ala Val Leu Pro Thr Val Ile Ile Cys Val Met Val
169                  245                 250                 255
170  Phe Cys Leu Ile Leu Trp Lys Trp Lys Lys Lys Lys Arg Pro Arg Asn
171              260                 265                 270
172  Ser Tyr Lys Cys Gly Thr Asn Thr Met Glu Arg Glu Glu Ser Glu Glu
173          275                 280                 285
174  Thr Lys Lys Arg Glu Lys Ile His Ile Pro Glu Arg Ser Asp Glu Ala
175      290                 295                 300
176  Gln Arg Val Phe Lys Ser Ser Lys Thr Ser Ser Cys Asp Lys Ser Asp
177  305                 310                 315                 320
178  Thr Cys Phe
181 <210> SEQ ID NO: 5
182 <211> LENGTH: 924
183 <212> TYPE: DNA
184 <213> ORGANISM: Homo Sapiens
186 <400> SEQUENCE: 5
187  atgggggcc tgacagcctc ggacgtacac ccgaccctgg gggtccagct cttctcagct      60
188  ggaatagcgg cgtgcttggc ggacgtgatc accttcccgc tggacacggc caaagtccgg     120
189  ctccaggtcc aaggtgaatg cccgacgtcc agtgttatta ggtataaagg tgtcctggga     180
190  acaatcaccg ctgtggtaaa aacagaaggg cggatgaaac tctacagcgg gctgcctgcg     240
191  gggcttcagc ggcaaatcag ctccgcctct ctcaggatcg gcctctacga cacggtccag     300
192  gagttcctca ccgcagggaa agaaacagca cctagtttag gaagcaagat tttagctggt     360
193  ctaacgactg gaggagtggc agtattcatt gggcaaccca cagaggtcgt gaaagtcaga     420
194  cttcaagcac agagccatct ccacggaatc aaacctcgct acacggggac ttataatgcg     480
195  tacagaataa tagcaacaac cgaaggcttg acgggtcttt ggaaagggac tactcccaat     540
196  ctgatgagaa gtgtcatcat caattgtaca gagctagtaa catatgatct aatgaaggag     600
197  gcctttgtga aaaacaacat attagcagat gacgtcccct gccacttggt gtcggctctt     660
198  atcgctggat tttgcgcaac agctatgtcc tccccggtgg atgtagtaaa aaccagattt     720
199  attaattctc caccaggaca gtacaaaagt gtgcccaact gtgcaatgaa agtgttcact     780
200  aacgaaggac caacggcttt cttcaagggg ttggtacctt ccttcttgcg acttggatcc     840
201  tggaacgtca ttatgtttgt gtgctttgaa caactgaaac gagaactgtc aaagtcaagg     900
202  cagactatgg actgtgccac ataa                                           924
204 <210> SEQ ID NO: 6
205 <211> LENGTH: 307
206 <212> TYPE: PRT
207 <213> ORGANISM: Homo Sapiens
209 <400> SEQUENCE: 6
210  Met Gly Gly Leu Thr Ala Ser Asp Val His Pro Thr Leu Gly Val Gln
211   1               5                  10                  15
212  Leu Phe Ser Ala Gly Ile Ala Ala Cys Leu Ala Asp Val Ile Thr Phe
213              20                  25                  30
214  Pro Leu Asp Thr Ala Lys Val Arg Leu Gln Val Gln Gly Glu Cys Pro
215          35                  40                  45
216  Thr Ser Ser Val Ile Arg Tyr Lys Gly Val Leu Gly Thr Ile Thr Ala
217      50                  55                  60
```

RAW SEQUENCE LISTING DATE: 11/29/2000
PATENT APPLICATION: US/09/711,022 TIME: 09:12:34

Input Set : A:\V1397028.txt
Output Set: N:\CRF3\11292000\I711022.raw

```
218  Val Val Lys Thr Glu Gly Arg Met Lys Leu Tyr Ser Gly Leu Pro Ala
219  65                  70                  75                  80
220  Gly Leu Gln Arg Gln Ile Ser Ser Ala Ser Leu Arg Ile Gly Leu Tyr
221                  85                  90                  95
222  Asp Thr Val Gln Glu Phe Leu Thr Ala Gly Lys Glu Thr Ala Pro Ser
223              100                 105                 110
224  Leu Gly Ser Lys Ile Leu Ala Gly Leu Thr Thr Gly Gly Val Ala Val
225          115                 120                 125
226  Phe Ile Gly Gln Pro Thr Glu Val Val Lys Val Arg Leu Gln Ala Gln
227      130                 135                 140
228  Ser His Leu His Gly Ile Lys Pro Arg Tyr Thr Gly Thr Tyr Asn Ala
229  145                 150                 155                 160
230  Tyr Arg Ile Ile Ala Thr Thr Glu Gly Leu Thr Gly Leu Trp Lys Gly
231                  165                 170                 175
232  Thr Thr Pro Asn Leu Met Arg Ser Val Ile Ile Asn Cys Thr Glu Leu
233              180                 185                 190
234  Val Thr Tyr Asp Leu Met Lys Glu Ala Phe Val Lys Asn Asn Ile Leu
235          195                 200                 205
236  Ala Asp Asp Val Pro Cys His Leu Val Ser Ala Leu Ile Ala Gly Phe
237      210                 215                 220
238  Cys Ala Thr Ala Met Ser Ser Pro Val Asp Val Val Lys Thr Arg Phe
239  225                 230                 235                 240
240  Ile Asn Ser Pro Pro Gly Gln Tyr Lys Ser Val Pro Asn Cys Ala Met
241                  245                 250                 255
242  Lys Val Phe Thr Asn Glu Gly Pro Thr Ala Phe Phe Lys Gly Leu Val
243              260                 265                 270
244  Pro Ser Phe Leu Arg Leu Gly Ser Trp Asn Val Ile Met Phe Val Cys
245          275                 280                 285
246  Phe Glu Gln Leu Lys Arg Glu Leu Ser Lys Ser Arg Gln Thr Met Asp
247      290                 295                 300
248  Cys Ala Thr
249  305
251 <210> SEQ ID NO: 7
252 <211> LENGTH: 1105
253 <212> TYPE: DNA
254 <213> ORGANISM: Homo Sapiens
256 <400> SEQUENCE: 7
257  gttcctctat ctcgtcttgt tgctgattaa aggtgcccct gtctccagtt tttctccatc      60
258  tcctgggacg tagcaggaaa tcagcatcat ggttgggttc aaggccacag atgtgccccc     120
259  tactgccact gtgaagtttc ttggggctgg cacagctgcc tgcatcgcag atctcatcac     180
260  ctttcctctg gatactgcta aagtccggtt acagatccaa ggagaaagtc aggggccagt     240
261  gcgcgctaca gccagcgccc agtaccgcgg tgtgatgggc accattctga ccatggtgcg     300
262  tactgagggc ccccgaagcc tctacaatgg gctggttgcc ggcctgcagc gccaaatgag     360
263  ctttgcctct gtccgcatcg gcctgtatga ttctgtcaaa cagttctaca ccaagggctc     420
264  tgagcatgcc agcattggga gccgcctcct agcaggcagc accacaggtg ccctggctgt     480
265  ggctgtggcc cagcccacgg atgtggtaaa ggtccgattc caagctcagg cccgggctgg     540
266  aggtggtcgg agataccaaa gcaccgtcaa tgcctacaag accattgccc gagaggaagg     600
267  gttccggggc ctctggaaag ggacctctcc caatgttgct cgtaatgcca ttgtcaactg     660
268  tgctgagctg gtgacctatg acctcatcaa ggatgccctc ctgaaagcca acctcatgac     720
```

VERIFICATION SUMMARY DATE: 11/29/2000
PATENT APPLICATION: US/09/711,022 TIME: 09:12:35

Input Set : A:\V1397028.txt
Output Set: N:\CRF3\11292000\I711022.raw

L:13 M:270 C: Current Application Number differs, Replaced Current Application No
L:13 M:271 C: Current Filing Date differs, Replaced Current Filing Date

~~23. The method of claim 18, wherein the MHC class II HLA-DR inducing agent~~ is adriamycin.

24. The method of claim 18, wherein the MHC class II HLA-DR inducing agent is gamma interferon.

25. The method of claim 18, wherein the MHC class II HLA-DR inducing agent is selected from the group consisting of a UCR expression vector, a TCRαβ engagement molecule and a fatty acid.

26. The method of claim 18, wherein the endogenous MHC class II HLA-DR ligand is an MHC class II HLA-DR expressing cell.

27. The method of claim 18, wherein the MHC class II HLA-DR inducing agent is administered orally.

28. The method of claim 18, wherein the MHC class II HLA-DR inducing agent ~~is administered locally.~~

29. A method for inducing apoptosis in a tumor cell, comprising:

contacting a tumor cell with an amount of a metabolic modifying agent, which when exposed to a cell causes coupling of electron transport and oxidative phosphorylation, effective to increase the mitochondrial membrane potential in the tumor cell, and

contacting the tumor cell with an amount of an apoptotic chemotherapeutic agent effective for inducing apoptosis in the tumor cell.

30. The method of claim 29, wherein the metabolic modifying agent is glucose.

31. The method of claim 29, wherein the metabolic modifying agent is an MHC class II HLA-DP/DQ ligand.

32. The method of claim 29, wherein the metabolic modifying agent is selected from the group consisting of phorbol myristate acetate in combination with ionomycin, GDP, CD40 binding peptide, sodium acetate, UCP antisense, dominant negative UCP,, and staurosporine.

33. The method of claim 29, wherein the metabolic modifying agent is GDP.

34. The method of claim 29, wherein the apoptotic chemotherapeutic agent is selected from the group consisting of adriamycin, cytarabine, doxorubicin, and methotrexate.

35. The method of claim 29, wherein the metabolic modifying agent and the apoptotic chemotherapeutic agent are administered simultaneously.

36. The method of claim 29, wherein the metabolic modifying agent and the apoptotic chemotherapeutic agent are administered locally.

37. The method of claim 35, wherein the tumor cell is resistant to the apoptotic chemotherapeutic agent.

38. The method of claim 29, wherein the tumor cell is sensitive to the apoptotic chemotherapeutic agent, and wherein the amount of metabolic modifying agent is effective to increase mitochondrial membrane potential and the amount of apoptotic chemotherapeutic agent is effective to inhibit the proliferation of the tumor cell when the mitochondrial membrane potential is increased.

~~39. A method for decreasing mitochondrial membrane potential in a cell of a~~ subject, comprising

administering an MHC class II ~~HLA~~-DR ligand to the subject to selectively engage MHC class II HLA-DR on the surface of the cell ~~in an~~ amount effective to decrease ~~mitochondrial membrane potential in the mammalian cell.~~